Phase 2

Introduction

Phase 1 resulted in a list of 177 potential Chemicals of High Concern for Children (CHCCs). To further narrow down the number of chemicals we developed the Phase 2 prioritization scheme. Phase 2 is a child-centric qualitative assessment of toxicity and potential for exposure in an attempt to focus the potential CHCCs on chemicals of highest concern to children. Phase 3 will further document each chemical in a detailed written justification. An overview of the entire process is described in the executive summary.

Ecology and DOH contracted with Dr. Catherine Karr (University of Washington Pediatric Environmental Health Specialty Unit) to provide scientific and technical advice regarding the development of the process for prioritizing CHCCs. Dr. Karr developed a framework that allowed us to quickly assess and prioritize chemicals. Ecology adapted the framework, presented below, to develop a score sheet for each chemical being considered.

The chemical prioritization scheme is designed to respond to the following question:

What is the degree of concern that children's current or future health status will be compromised if they are exposed to this potential CHCC through its use in children's products?

In concept, CHCCs should be those chemicals that are the most likely to cause the most harm to the most children, but we do not have enough information for a thorough chemical-by-chemical quantitative risk assessment. Therefore, we used an evaluation process that provides a qualitative and relative ranking of highest, medium or lower concern. Core principles in children's environmental health and risk assessment (children's risk differs because of their developing and differentiating tissues and organs and they have different exposure patterns than adults) were considered in developing a prioritization approach.[1] [2]

Two decision-making frameworks provide a focus on toxicity endpoints of concern for child health and exposure routes and pathways relevant to children. Results from each framework were then entered into a matrix to evaluate higher vs. lower level of priority for chemicals in children's products.

- **Toxicity** – The body of information on child health and reproductive toxicity endpoint was categorized based on weight of evidence for each potential CHCC. All the potential CHCCs being prioritized have already been screened for toxicity, although the extent of toxicity evaluation is not the same for each. The scores, called "Worst, Severe, and Bad," reflect this difference where the "worst" chemicals are those where human toxicity is best documented.

- **Exposure** - Similarly, information regarding potential for exposure among children for each chemical was evaluated and potential CHCCs were categorized. Considerations included both the individual child's potential for exposure to the chemical from its use in a child product and the number of children likely exposed to this chemical from products containing it. This incorporates the potential for exposure via multiple products/sources and opportunity for a large number of children to be affected. The potential for exposure to the CHCCs were categorized as "Known, Possible or Unlikely." Again, this categorization was based on the weight of the evidence.

For both toxicity and potential for exposure, categorization was based on peer-reviewed evidence where such data were available and informative. In general toxicity data are better documented than exposure data. However, there are data quality issues for both toxicity and exposure data. In addition, the quality and quantity of the data vary across chemicals in commerce. As such, conducting risk assessments is problematic when there is inadequate toxicity or exposure data for consumer products. A chemical was only considered to not have a toxicity endpoint if it had been assessed and found not to possess that toxicity endpoint. If a chemical had not been assessed, or if there was insufficient information to make a decision, then the chemical was scored as "no information" or "NI." Similarly, a chemical was only considered to not be in a product if it had been looked for and not found. If no information was found, then the chemical was scored as NI.

For each chemical, the toxicity and exposure rankings were combined through a simple hazard matrix. Figure 1 shows the hazard matrix.

		EXPOSURE Rank		
		Known	**Possible**	**Unlikely**
TOXICITY Rank	**Worst**	**W/K**	**W/P**	**W/U**
	Severe	**S/K**	**S/P**	**S/U**
	Bad	**B/K**	**B/P**	**B/U**

Figure 1. Hazard Matrix

This approach can be applied to any candidates for the list of CHCCs. It may also be employed, with slight modifications, in an ongoing manner as new and existing chemicals are found in children's products, or as available data on existing chemicals is enriched. The first use of Phase 2 reflects that these 177 chemicals have already been identified in Phase 1 as both toxic and having the potential for exposure, as defined in the CSPA.

Incorporating a Children's Environmental Health Framework

Several states, nations, and international agreements acknowledge the benefits of enhanced product safety and this has stimulated the development of a number of approaches to identify and prioritize hazardous chemicals in manufactured goods. With the exception of a similar Child Safe Product Act in Maine (LD 2048 - Kids Safe Products Act), we identified no other chemical prioritization activities focused specifically on exposures from children's consumer products. However, the methods described for several recent and ongoing efforts with broader mandates including the European Union REACH program[3], the Canadian Environmental Protection Agency Final Integrated Framework[4], and the U.S. Environmental Protection Agency's ChAMP were reviewed for relevant concepts[5].

Evaluating child toxicity of a chemical

The framework for ranking child-centric toxicity considers the following core components:

- Evidence describing the chemical with respect to endpoints of highest concern for children: developmental toxicity, reproductive health, endocrine disruption, cancer.
- Strength and weight of the evidence for those health endpoints.

Environmental chemical exposures are among the multiple risk factors identified for the leading chronic health conditions affecting U.S. children.[6] Those that are among the most prevalent and have the highest increases in rates in recent decades are obesity, ADHD, and asthma.[7] [8] [9] The leading causes of mortality in early childhood are premature birth and congenital malformations.[10] Cancer, although rare in children, is the leading cause of pediatric disease mortality for children from infancy to age 15 years.[11]

Compared to adults, from the fetal period until adulthood, the child experiences rapid ongoing organ system development and a long potential lifespan that may allow time for latent development of chronic disease. Based on this, the chemicals of primary concern include those that interfere with the normal development or function of cells, organs and their organ systems in addition to those that are potential carcinogens.

A chemical may be associated with multiple child health consequences. This may occur via multiple toxicological mechanisms affecting different organs or systems, or via a single mechanism that influences the development or function of multiple end organs or systems. The need to address the life-stages in risk assessment for child health is increasingly recognized.[12] [13] The emerging life-stage paradigm recognizes that health outcomes or risk from exposures during growth and development will not be necessarily the same for all life stages. The outcomes will depend on the underlying developmental processes that determine susceptibility at the time of exposure. Increasingly, it is recognized that fetal and childhood stages are critical developmental periods for virtually all tissues, organs, and systems and increased sensitivity to harmful exposures during these periods is of concern for immediate and latent adverse health outcomes including

cancer and reproductive health. For example, perturbations of these developmental processes by environmental toxicants may compromise the health and development of children, which manifest as chronic lifelong conditions such as birth defects, asthma, learning disabilities, as well as future fertility. Further discussion and examples of this have been described in several reviews.[6 7 14]

Based on the current state of knowledge regarding the public health burden of pediatric morbidities and physiological vulnerabilities of children, it is particularly important to identify developmental toxicants. Chemicals with mechanisms that are associated with carcinogenesis are also of high concern in children because cells that undergo carcinogenic transformation in childhood have more time to develop into tumors than those occurring in adults. This is reflected in U.S. EPA's Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens.[14] In addition, the science and policy surrounding chemicals that have endocrine disrupting (ED) properties is expanding rapidly in response to increasing concerns for adverse health consequences in humans as well as the environment.[15 16] For example, *in utero* and early childhood exposures to EDs may be responsible, at least in part, for decreases in semen quality; increasing incidence of congenital malformations of the reproductive organs, such as hypospadias; increasing incidence of testicular cancer; and acceleration of onset of puberty in females.[17] As such, EDs have mechanistic properties that may influence developmental health, reproductive health, and/ or cancer. Due to the relative infancy of this field and its increasing prominence in child environmental health policy and research, it is useful to characterize this mechanism of toxicity end point distinctly.

The toxicity evaluation focuses on the strength and weight of evidence for these toxicological endpoints. All of the potential CHCCs in Phase 2 were screened for toxicity in Phase 1, so there is some known toxicity. The evaluation in Phase 2 is based on the strength of the evidence.

Evaluating potential for exposure of a child to a chemical in a product

In addition to evaluating the child health toxicity of chemicals that may be in children's products, it is critical to consider the other features that will influence the risk of harm for any individual child or the population of children – specifically the opportunity for that chemical to be taken up by the child and absorbed such that a potentially toxic dose could be delivered. Unfortunately, data informative of such exposure is currently limited, non-uniform and imperfect. One of the purposes of the law is to help gather this type of information.

The agencies have selected reliable information sources for identifying the presence of a chemical in human biomonitoring data, indoor air/dust data, drinking water data, or children's product data. These types of data were used in Phase 1 as a broad screen to represent opportunity and evidence of potential exposure for children. In Phase 2 we examined these and additional proxy data sources to further hone in on the potential for exposure to chemicals in children's products.

Proxy data sources provide information in the absence of more optimal data. For example, inhalation exposure risk may be gauged from chemical parameters such as vapor pressure (proxy) rather than measures of concentrations in breathing zone air when the product is used by children (more optimal). Dermal exposure risk may be extrapolated from product type and use such as whether it is applied directly to skin (proxy) rather than data on dermal absorption during child use of the product (more optimal).

Phase 2 focuses specifically on potential exposure pathways most relevant to the child's encounter with a product containing the chemical and does not address the potential for exposure and harm upstream or downstream of child product use. For example, this framework does not include exposures that result from manufacture and distribution or disposal of the chemical or child product. Significant occupational exposures or community contamination including soil, food supply, and water may occur related to these features of the chemical or product lifespan but are not addressed here since the prioritization focuses on exposures to children from the use of children's products.

Opportunity for exposure to a hazardous chemical in a child or consumer product depends on many factors including presence of the chemical in the product, the availability of the chemical to transfer from the product to the child either through direct contact or indirectly (i.e. product residues left in the child's ambient environments or leached into foodstuffs), and the extent to which harmful interaction with the body may occur. Features of the *chemical's behavior* as well as *features of the product's construction and use*, intended or unintended, will influence the child's opportunity for exposure and uptake. Child age and behaviors such as mouthing will also influence route and extent of potential exposure. Available data or proxy data to represent these features were considered in determining which chemicals have the greatest exposure potential and should be ranked as higher priority.

Two perspectives of exposure concern were considered. These include the risk to an individual child. Also, it is important to evaluate the exposure potential to the population of children from the chemical being in multiple children's products or consumer products in general. The individual child exposure risk perspective represents the potential for some children to have very high exposures and thus more likely to be harmed. The population of children exposure risk perspective represents the potential for many or most children to be exposed and thus the likelihood of some children experiencing harm is increased.

A set of data sources was used for chemical and product information. Also standard user behavior information was used to determine whether a chemical should be placed in a known, possible or unlikely category for potential exposure concern. Given the heterogeneity of the quality and quantity of relevant information for assessing the presence of chemicals in children or consumer products and the exposure to the child from use of those products, the determinations among the decision points represent largely qualitative assessments regarding the available body of information. Where information from peer-reviewed, authoritative scientific or regulatory bodies is available, they were considered with greater weight than data from stakeholder groups such as consumer organizations or manufacturers.

Limitations

The challenges of designing a best assessment within the constraints of data quality and availability and Agency resources are significant. In general, it is important to recognize that the approach described is not intended to be a chemical by chemical exhaustive primary literature review with critical evaluation of all studies with a quantitative risk assessment for each chemical-product combination. The limitations of the current evidence base make such a “gold standard” unrealistic. Phase 3 will further investigate each chemical that is likely to be on the reporting list, but will not be a full literature review or quantitative risk assessment.

The approach taken leverages the existing processes of authoritative bodies that are tasked with aspects of chemical health risk assessment, gleaning components with relevance to this task of prioritizing chemicals of high concern to children in children’s products. One important challenge is that we don’t know what chemicals are likely to be in children’s products, outside of some chemicals that have been found in children’s products. Many concepts are not included that may influence toxicity and vulnerability; such as specific ages of child product users, concentration of chemicals in products, genetic variations in disease susceptibility and metabolism, structure activity relationships among chemicals, etc. Phases 1 and 2 both relied heavily on older, established lists, yet the evidence base is evolving. In recognition of this fact and because developmental and endocrine disruption are particularly important endpoints for children, this framework gives priority to such chemicals.

The intent of the approach is to provide guidance toward a relatively efficient but scientifically sound process of prioritization to protect the public’s health despite these recognized limitations.

Phase 2 details

Phase 2 used an algorithm to rank potential CHCCs with information from a set of sources. It was not a comprehensive review of all information available, but was limited to the identified set of sources. For transparency and recordkeeping, a summarized qualitative score sheet that outlines this information was prepared for each chemical. Figure 2 shows the template for the score sheet. Phase 2 uses many of the same sources of information that were used in Phase 1. A description of each source that was used for Phase 2 is included at the end of this document after the references. Some information on an individual chemical could be found in more than one of the sources.

Chemical: _____ **CAS:** _____

Toxicity

I. Developmental or Reproductive Toxicity	Worst	Severe	Bad	No	No Info	Value or Comment
1. Prop 65						
Identified as developmental or reproductive toxicant	Yes				NI	
2. NTP CERHR finding						
Clear or some evidence of adverse effects in humans	Yes					
Limited evidence in humans or some evidence in animals		Yes				
Limited evidence in animals			Yes			
Some or clear evidence of no observable adverse effects				Yes		
3. EU Existing Substances						
Identified as Category 1, 2 or 3	Cat 1	Cat 2	Cat 3		NI	
4. GHS						
Identified as Category 1A, 1B or 2 for reproductive toxicity or germ cell mutagenicity	Cat 1A	Cat 1B	Cat 2		NI	
5. REPROTEXT						
Rated as A^{+}, A, A^{-}, B^{+}, B, B^{-}, C, D, E, F	A+, A	A-, B+	B	E, F	B^{-}, C, D, NR	
6. LOAEL or RTECS TDLo or TCLo						
Oral value (mg/kg-bw/day)	< 50	≥ 50 - ≤ 250	> 250		NI	
Dermal value (mg/kg-bw/day)	< 100	≥ 100 - ≤ 500	> 500		NI	
Inhalation (vapor) value (mg/L/day)	< 1.0	≥ 1.0 - ≤ 2.5	> 2.5		NI	
Inhalation (dust/mist/fume) value (mg/L/day)	< 0.1	≥ 0.1 - ≤ 0.5	> 0.5		NI	
Inhalation (gas) value (ppm/day)	< 50	≥ 50 - ≤ 250	> 250		NI	

Final Dev. & Repro. Determination

II. Endocrine Disruption	Worst	Severe	Bad	No	No Info	Value or Comment
7. EU Endocrine Disruptor Program						
Identified as Category 1 or 2	Cat 1	Cat 2			NI	

Final ED Determination

III. Carcinogenicity	Worst	Severe	Bad	No	No Info	Value or Comment
8. IARC						
Identified as Category 1, 2A, 2B, 3, 4	Cat 1	Cat 2A	Cat 2B	Cat 4	Cat 3 or NI	
9. NTP						
Identified as known or reasonably anticipated	Known	Anticipated			NI	
10. EPA IRIS						
Identified in 1986 criteria	Cat A	Cat B1 or B2	Cat C	Cat E	Cat D or NI	
Identified in 1996 criteria	KNO			UNL	UNK or NI	
Identified in 1999 criteria	KNO	LIK	SUG	UNL	INA or NI	
Identified in 2005 criteria	KNO	LIK	SUG	UNL	INA or NI	
11. EU Carcinogen list						
Identified as Category 1 or 2	Cat 1	Cat 2			NI	
12. GHS						
Identified as Category 1A, 1B or 2 for carcinogenicity	Cat 1A	Cat 1B	Cat 2		NI	
13. Proposition 65 list						
Identified as a carcinogen		Yes			NI	

Final Carc. Determination

Final Toxicity Determination

Comments

Chemical: _____ **CAS:** _____

Exposure

I. Presence in a Child Product	Known	Possible	Unlikely	No Info	Value or Comment
14. Found in Danish EPA or Dutch studies and reports	Yes		Not found	NI	
15. EU or authoritative Risk Assessment indicating use in children's products	Yes	Yes	Not found	NI	
16. Evidence in data in HSDB indicating use in children's products		Yes	Not found	NI	
17. Environmental Working Group database use in children's products		Yes	Not found	NI	
18. EPA's Inventory Use and Reporting database (IUR) indicating use in children's products		Yes	Not found	NI	
19. NLM Household products database indicating use in children's products		Yes	Not found	NI	

Final Child Prod. Determination

II. Potential for Individual Child Exposure	Known	Possible	Unlikely	No Info	Value or Comment
20. Do Danish and Dutch studies or any authoritative risk assessment indicate any exposure potential for children?	Yes			NI	
21. Does the ChAMP program indicate any exposure potential for children?	Yes			NI	
22. Is the chemical included in EPA's VCCEP?		Yes		NI	
23. Inhalation					
Is the product type or use likely to release toxics into the air?	Yes			NI	
- What is the chemical's vapor pressure (mmHg at 25 degrees C)?		≥ 1	< 1	NI	
24. Ingestion or Mouthed or Sucked by children					
Is product type or use likely ingested or mouthed or sucked by children?	Yes			NI	
- What is the chemical's water solubility (mg/L) at 25°C?		≥ 1,000	< 1,000	NI	
25. Dermal					
Is product type or use likely applied to, be absorbed into or remain in contact with skin?	Yes			NI	
- How long does the product remain in contact with the skin?	> 1hr	> 3 min - < 1hr	< 3 min	NI	

Final Ind. Exp. Determination

III. Potential for Population Exposure	Known	Possible	Unlikely	No Info	Value or Comment
26. Is the chemical found in the NHANES biomonitoring studies?	Yes		Not found	NI	
27. Is the chemical found in consumer and household products?		Yes	Not present	NI	
28. Is the chemical found in indoor house dust and air?		Yes	Not present	NI	
29. PBT Characteristics					
Is the chemical on Ecology's PBT list?	Yes			NI	
- What is its half-life in water, soil or sediment (months)?		≥ 6	< 6	NI	
- What is its half-life in air (days)?		>2	< 2	NI	
- What is its bioconcentration factor?		≥ 5000	< 5,000	NI	
30. Amount produced (lbs)/yr based on HSDB, IUR & HPV data?		≥ 1,000,000	< 1,000,000	NI	

Final Pop. Exp. Determination

Final Exposure Determination

Comments

Figure 2. Score Sheet

Child-Centric Toxicity

Prioritization is based upon an evidence review summary for three toxicity endpoints:

I. Developmental and reproductive system toxicity
II. Endocrine disruption potential
III. Carcinogenicity

Figure 3 shows the decision making framework for toxicity. If a chemical is put into the worst category for any of the toxicity endpoints, it is considered to be in the worst category for toxicity overall. If a chemical is put into the bad category for all of the toxicity endpoints, it is considered in the bad category for toxicity overall. The rest are placed in the severe category for toxicity.

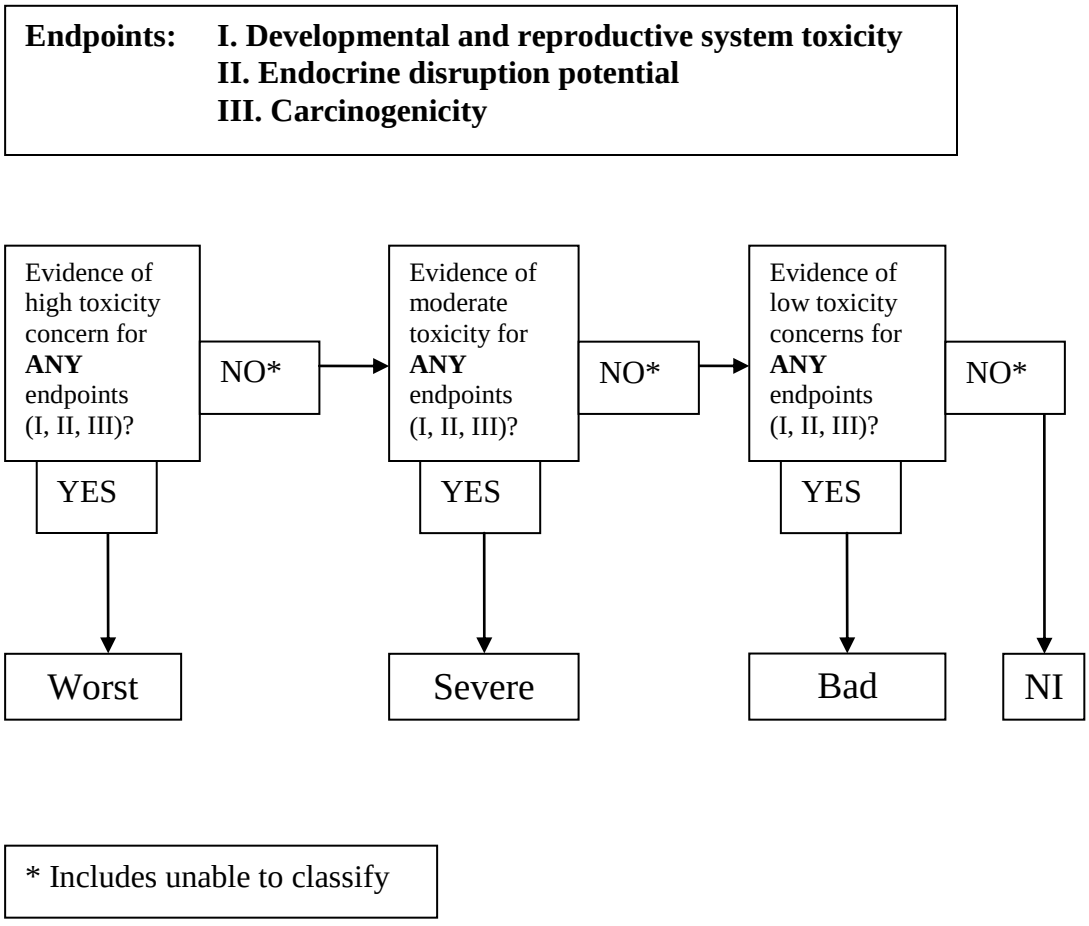

Figure 3. Decision-making Framework for Child Toxicity

I. Evidence regarding potential developmental or reproductive toxicity

Developmental toxicity includes adverse consequences on survival or normal development or function of organs and organ systems including congenital malformations due to exposure during fetal life and/or childhood. Reproductive toxicity is specifically adverse consequences on the development or function of the reproductive system.

Historically, in both scientific processes and policy arenas, developmental and reproductive toxicity have been considered together.[1 18 19] These outcomes reflect a spectrum and cycle of adverse consequences that range from fertility to delivery to postnatal growth and development of a child to healthy reproductive capacity in adulthood.

The following are recommended and reputable sources that provide a scientifically-driven, relatively up to date, weight of evidence approach which provides an efficient screen for defining whether developmental or reproductive toxicity concern has been identified for a particular chemical. For each decision point, the sources indicated were used to place potential CHCCs in the respective categories.

Worst

- Listed as California Prop 65 developmental or reproductive toxicant
- Evaluated by National Toxicology Program (NTP) Center for Evaluation of Risks to Human Reproduction (CERHR) with findings that the chemical has clear or some evidence of adverse effects in humans.
- Identified by European Union as toxic to reproduction or mutagenic in Category 1.
- Identified by the Global Harmonization System (GHS) as category 1A for reproductive toxicity or germ cell mutagenicity.
- Rated in REPROTEXT as A+ or A.
- Has a LOAEL or RTECS TDLo or TCLo
    - Oral value (mg/kg/day) < 50
    - Dermal value (mg/kg/day) <100
    - Inhalation (vapor) value (mg/L/day) <1.0
    - Inhalation (dust/mist/fume) value (mg/L/day) <0.1
    - Inhalation (gas) value (ppm/day) <50

Severe

- Evaluated by NTP CERHR with findings that the chemical has limited evidence in humans or some evidence in animals.
- Identified by European Union as toxic to reproduction or mutagenic in Category 2.
- Identified by the Global Harmonization System (GHS) as category 1B for reproductive toxicity or germ cell mutagenicity.
- Rated in REPROTEXT as A- or B+.
- Has a LOAEL or RTECS TDLo or TCLo

    - Oral value (mg/kg/day) between 50 and 250
    - Dermal value (mg/kg/day) between 100 and 500
    - Inhalation (vapor) value (mg/L/day) between 1 .0 and 2.5
    - Inhalation (dust/mist/fume) value (mg/L/day) between 0.1 and 0.5
    - Inhalation (gas) value (ppm/day) between 50 and 250

Bad

- Identified by Prop 65 review process not to meet the criteria for developmental or reproductive toxicity
- Evaluated by NTP CERHR with finding of limited evidence in animals.
- Identified by European Union as toxic to reproduction or mutagenic in Category 3.
- Identified by the Global Harmonization System (GHS) as category 2 for reproductive toxicity or germ cell mutagenicity.
- REPROTEXT rating of B.
- Has a LOAEL or RTECS TDLo or TCLo
    - Oral value (mg/kg/day) > 250
    - Dermal value (mg/kg/day) > 500
    - Inhalation (vapor) value (mg/L/day) > 2.5
    - Inhalation (dust/mist/fume) value (mg/L/day) >0.5
    - Inhalation (gas) value (ppm/day) > 250

No

- Evaluated by NTP CERHR with finding of some or clear evidence of no observable adverse.
- REPROTEXT rating of E or F.

No Information

- REPROTEXT rating of B-, C, D, or not rated (NR)
- No information about the chemical in the source.

The purpose of using lowest observed adverse effect levels (LOAELs) from the ATSDR toxicological profiles or lowest toxic dose/concentration (TDLo/TCLo) from Registry of Toxic Effects of Chemical Substances (RTECS)was to identify chemicals with developmental or reproductive toxicity that are not on the authoritative lists, especially chemicals with newer information in this toxicity endpoint. The ranges that were used are from EPA Chemical Assessment and Management Program (ChAMP).[5] If this was the only information on this endpoint, the potential CHCC was flagged for further evaluation in Phase 3.

II. Evidence regarding endocrine disruption

For the purposes of this prioritization, endocrine disruption evidence is considered separately, even though the end organs and systems affected may include reproductive function, developmental health and/or other toxicity endpoints such as cancer or immunotoxicity.

The European Union evaluation of endocrine disrupting chemicals provides an accessible weight of evidence based listing of endocrine disrupting chemicals. With ongoing high interest in developing this evidence base, in the future there may be additional authoritative body and scientific reviews available for consideration.

Worst

- Identified as EU endocrine disrupting chemical in Category 1.

Severe

- Identified as EU endocrine disrupting chemical in Category 2.

No Information

- No information about the chemical on the EU priority list for endocrine disrupters.

III. Evidence regarding carcinogenicity

Historically, the focus on carcinogenicity testing has exceeded developmental, reproductive and endocrine disruption toxicity screening and evaluation. As such, there is generally more data available on this endpoint and more available weight of evidence ranking by reputable and authoritative sources.

The following are recommended and reputable sources that provide a scientifically-driven, relatively up to date, weight of evidence approach which provides an efficient screen for defining whether cancer concern has been identified for a particular chemical. California does not use the same distinctions in the weight of evidence to place chemicals on the Prop 65 carcinogen list, so presence on the Prop 65 list of carcinogens was used to place potential CHCCs in our “Severe” category rather than in the “Worst” category.

Worst

- IARC 1
- NTP Known
- EPA IRIS A or Known
- EU Category 1
- GHS Category 1A

Severe

- IARC 2A
- NTP reasonably anticipated
- EPA IRIS B1 or B2, or Likely
- EU Category 2
- GHS Category 1B
- Identified by Prop 65 review process to meet the criteria for carcinogenicity

Bad

- IARC 2B (possibly carcinogenic to human)

- EPA IRIS C or Suggested
- GHS Category 2

No

- IARC 4
- EPA IRIS E or Unlikely

No Information

- IARC 3
- EPA IRIS D or Inadequate information
- No information about the chemical in the source.

Decision-making Framework for Ranking Child Potential for Exposure

Prioritization for exposure is based on three decision points:

I. Presence in a children's product
II. Individual exposure
III. Population exposure

There is considerable heterogeneity in quality, specificity, and quantity of relevant information for assessing the presence of chemicals in children or consumer products and the exposure to the child from use of those products. Unlike the toxicity priority ranking, the determinations for exposure ranking require a large reliance on proxy information that is often somewhat distal to the information desired.

Figure 4 shows the decision making framework for potential for exposure. The process is different than for toxicity. In decision point I, a chemical is put in an initial category based on whether it is Known, Possible or Unlikely to be in children's products. In decision point II, that category may be raised or lowered based on the potential for exposure to a child during use of a product that contains the chemical. In decision point III, the category may be raised or lowered based on the concern for widespread population level exposure to the chemical. This can be seen with formaldehyde (CAS 50-00-0) as an example (see appendix 1 for formaldehyde's score sheet). The Danish EPA found formaldehyde in children's products, so it is "Known" for the first decision point. Decision point II is also "Known," and there is no change because it is already in the highest category. The third decision point is "Possible," which does not change the category, so formaldehyde's final category is "Known."

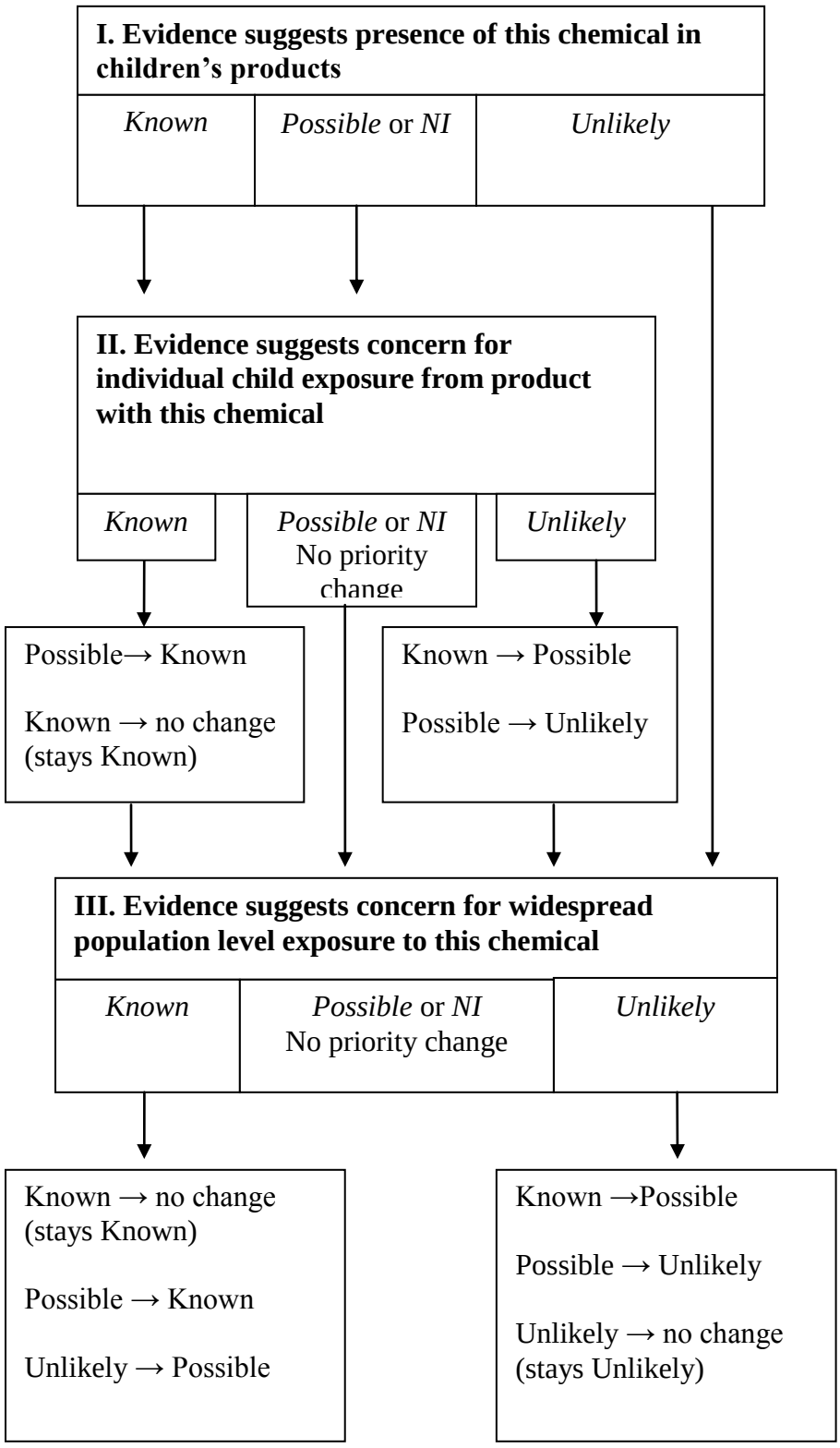

Figure 4. Decision-making Framework for Ranking Child Exposure Potential

I. Presence in a children's product

The first decision point is an assessment of evidence regarding whether or not a chemical is present in products designed for use by children. The sources below were used to determine the confidence with which a chemical is felt to be present in a children's product.

Known

- Danish EPA or Dutch studies and reports
- EU or authoritative risk assessment indicating use in children's products.

Possible

- Evidence or data in the Hazardous Substances Data Bank (HSDB) indicating possible use in children's products.
- EPA's Inventory Use and Reporting (IUR) database indicating use in children's products.
- National Library of Medicine Household Products Database indicating use in children's products. In addition to products that are clearly labeled as children's products, arts and crafts supplies and sunscreens were also considered to be children's products.
- Environmental Working Group (EWG) database of chemicals in cosmetics and sunscreens indicating use in children's products.

Unlikely

- A chemical is considered unlikely to be in children's products if it was looked for and not found.

No Information

- No information about the chemical in the information source.

Potential CHCCs that are known to be in children's products are assumed to be of high concern for exposure in children and are ranked as known- the top priority at the first decision step. Potential CHCCs that have some evidence to suggest they *could be* in children's products or for which there is inadequate information are assumed to be of some level of concern for exposure in children. In the absence of better information, these chemicals are ranked as middle priority, or possible, at this first decision step. If there is evidence or reliable information that the potential CHCC is not found in a children's product, the chemical is ranked as lowest priority, or unlikely, at this first decision point.

Chemicals which are determined to be known or possibly in children's products undergo further evaluation regarding a child's opportunity for exposure in encountering the product in decision point II. Chemicals that are unlikely to be in children's products proceeded to consideration of population level exposure for children to this chemical (see III below). Chemicals for which no information was available were considered to possibly be in children's products.

II. Potential for individual child exposure with use of products containing the chemical

The second decision point is designed to inform the extent of an individual child's possible exposure to a chemical. It is focused on the child's interaction with the chemical in a children's product.

Both *chemical* properties and *product* type and use may inform the ranking. Information relevant to potential exposures via inhalation, dermal, and ingestion routes were considered.

Many of the same sources used earlier are used to answer questions in this evaluation. For example, vapor pressure and water solubility data were usually obtained from HSDB. The same studies and reports from reputable, scientific or authoritative regulatory bodies were used here that were used to ascertain a chemicals presence in children's products.

Vapor pressure is a readily available component of chemical property information that serves as a surrogate for the opportunity for inhalation exposure. There is also available guidance on interpretation of vapor pressure with respect to inhalation risk. The U.S. EPA ChAMP documentation provides a scheme for interpreting vapor pressure as negligible, low, moderate, or high inhalation risk.[5]

Ingestion would be a potential route of exposure if the chemical is known or likely present in products designed to be placed in the mouth or likely to be used as chewing or sucking toys. All products for children younger than 3 years old are considered likely to be used as chewing or sucking toys. If the chemical is present in products that are used to store or contain food or beverages, this would be concerning for potential ingestion risk. Information on chemical water solubility may provide reassurance if the chemical meets established definitions of not likely to leach.

Support for likely dermal exposure would be indicated if the chemical was suspected or likely to be in products applied to the skin or that remain in prolonged contact with the skin and have a tendency to be absorbed through the skin.

Known

- Danish or Dutch studies or any authoritative risk assessment indicated any exposure potential for children
- EPA ChAMP program indicated any exposure potential for children
- Product type or use
    - Inhalation- perfumes, tents and tunnels
    - Ingestion- intended for children under the age of 3, mouthed or sucked, balloons, and food and beverage containers
    - Dermal- lotions, cosmetics and sunscreens.
- Product remains in contact with the skin for > 1hour

Possible

- Included in EPA's VCCEP

- Vapor pressure (mmHg) >1
- Water solubility (mg/L) at 25^{o}C >1000
- Product remains in contact with the skin for between 1hour and 3 minutes

Unlikely

- Vapor pressure (mmHg) <1
- Water solubility (mg/L) at 25^{o}C <1000
- Product remains in contact with the skin for < 3 minutes

No Information

- No information on the chemical from those sources

The ranking may increase or decrease depending on the information on individual exposure. If the information is deemed inadequate to be informative, no change in ranking is made.

III. Potential for population-wide exposure

The final decision point regarding potential for children's exposure includes concepts related to the population level opportunity to encounter the chemical. This incorporates the potential for exposure via multiple products/sources and opportunity for a large number of children to be affected.

The National Health and Nutrition Examination Survey (NHANES) is a collection of U.S. population biomonitoring studies which are representative of the population. There are many other biomonitoring studies, but they may not be representative of the U.S. population. On the score sheets we noted when a chemical was found in other biomonitoring studies used in Phase 1, but we did not use these studies in Phase 2 to score a potential CHCC as being found in human tissue.

Product information for population level exposure comes from the same sources as in the first decision point on presence in children's products, but encompasses a larger variety of consumer and household products. Proxy data for indoor residential environmental sampling on house dust and air contaminants is also used because chemicals from products may be in house dust and indoor air. These papers were used in the original screen for potential for exposure in Phase 1 and do not represent a full literature search.

Toxic chemicals that are persistent and bioaccumulate (PBTs) are considered in Washington to be the worst of the worst and to raise special challenges for our society and the environment. These chemicals are listed in the PBT Rule (173-333 WAC). In addition to our state's PBT list, we also used the criteria used by the EPA PBT Profiler to determine if chemicals were persistent and/or bioaccumulative.

Production volume is also used as a proxy for widespread exposure. Chemicals that are widespread in commerce meet the definition of U.S. EPA high production volume chemicals (i.e., manufactured or imported at > 1 million pounds per year).

Known

- Found in NHANES biomonitoring data
- On Washington's PBT list

Possible

- Found in consumer and household products
- Found in indoor house dust and air
- The half-life in water, soil or sediment is > 6 months
- The half-life in air is > 2 days
- The bioconcentration factor is >5000
- The annual production volume is >1,000,000 lbs, based on HSDB, IUR or high production volume (HPV) data.

Unlikely

- The half-life in water, soil or sediment is < 6 months
- The half-life in air is < 2 days
- The bioconcentration factor is <5000
- The annual production volume is <1,000,000 lbs, based on HSDB, IUR or HPV data.

Results of Phase 2

TOXICITY Score		EXPOSURE Score		
		Known	**Possible**	**Unlikely**
	Worst	**37**	**30**	**0**
	Severe	**25**	**44**	**0**
	Bad	**4**	**8**	**0**

Figure 5. Results of Phase 2

Figure 5 shows the results of Phase 2. The individual score sheets and a spreadsheet summarizing the individual results for the 177 potential CHCCs that were scored are included in the appendices 1 and 2. They are provided as a separate links on the web site. Not shown in Figure 5 are an additional 26 potential CHCCs that did not have known toxicity for the three endpoints in Phase 2, two potential CHCCs that did not have potential for exposure based on the Phase 2 prioritization process, and one that doesn't have toxicity or exposure information used in the Phase 2 algorithm. These 29 potential CHCCs all have toxicity and potential for exposure that meet the definitions in the law. However, for the purposes of the initial evaluation, these chemicals were removed from further consideration at this time.

The chemicals shaded in Figure 5 will undergo additional review in Phase 3. These potential CHCCs were selected because they all were identified as having a known potential for exposure to children. The final reporting list will be a subset of these potential CHCCs. In addition to the further toxicological and exposure review identified in Phase 3, each chemical will be evaluated to determine if an acceptable analytical technique exists and whether a acceptable reporting limit can be selected.

In addition, we decided to include all the persistent, bioaccumulative and toxic chemicals (PBTs) from the list of 177 potential CHCCs (adding 5 additional chemicals). These chemicals have already been identified as the “worst of the worst” and while the evidence of exposure is weak for a few of these chemicals, we want to know if they are in children’s products.

Annotated References for Sources used for Phase 2 Score Sheets

For access dates for web resources, see the Phase 1 references section.

ATSDR. http://www.atsdr.cdc.gov/. The Agency for Toxic Substances and Disease Registry (ATSDR) is a federal public health agency of the U.S. Department of Health and Human Services. ATSDR publishes toxicological profiles for hazardous substances found at National Priorities List sites, and for the Department of Defense and the Department of Energy. The toxicological profiles include information on hazard and exposure, including uses.

California Prop 65. http://www.oehha.org/prop65/prop65_list/Newlist.html. Hazard identification documents at: http://www.oehha.ca.gov/prop65/hazard_ident/hazard_id.html . Prop 65 list change documents: http://www.oehha.org/prop65/CRNR_notices/list_changes/index.html. Non-listed chemicals:
http://www.oehha.org/prop65/CRNR_notices/admin_listing/process_procedures/index.html
California Reference Exposure Levels for inhalation risks, table of:
http://www.oehha.org/air/allrels.html.
Proposition 65 (Prop 65), the Safe Drinking Water and Toxic Enforcement Act of 1986, was enacted as a California ballot initiative in November 1986. Prop 65 was intended by its authors to protect California citizens and the State's drinking water sources from chemical chemicals known to cause cancer, birth defects or other reproductive harm, and to inform citizens about exposures to such chemicals. Each year, the Office of Environment Health Hazard Assessment (OEHHA) section of the California EPA publishes an updated list of chemicals of concern. Some chemicals are included on the list based on other authoritative reviews, while others are listed based on a review of the available information by OEHHA.

Danish EPA. http://www.mst.dk/English/Chemicals/Consumer_Products/Surveys-on-chemicals-in-consumer-products.htm. The Danish Ministry of the Environment (EPA) conducted studies to identify chemical substances in a number of consumer products, including some specifically in children's products. Many of these reports have been translated into English. The Danish EPA analyzed the products for chemicals of concern. They also conducted off-gassing or leaching studies on many of the products and included these results in their reports. For example, in the reports on chemicals in tents and tunnels, the air space was sampled. A full list of references for these reports is in Phase 1.

Dutch Reports. The Dutch Food and Consumer Product Safety Authority and the Dutch Inspectorate for Health Protection and Veterinary Public Health have tested children's products for chemicals. A full list of references for these reports is in Phase 1.

EPA ChAMP. http://www.epa.gov/champ/. The EPA Chemical Assessment and Management Program (ChAMP) was designed to develop screening-level, hazard, exposure and risk characterizations for the 6,750 chemicals produced or imported in quantities of 25,000 lbs or greater a year. This includes High Production Volume (HPV) chemicals (greater than 1,000,000 lbs per year) and Medium Volume Production (MPV) chemicals (less than 1,000,000 lbs and greater than 25,000 lbs per year). ChAMP includes risk-based prioritization and hazard-based prioritizations. ChAMP has been superseded by a new approach that was announced on September 29, 2009.

EPA HPV Challenge. http://www.epa.gov/chemrtk/index.htm. HPV chemicals are classified as those chemicals produced or imported in the United States in quantities of 1 million pounds or more per year. Companies are "challenged" to make health and environmental effects data publicly available on HPV chemicals. As of June 2007, companies have sponsored more than 2,200 HPV chemicals, with approximately 1,400 chemicals sponsored directly through the HPV Challenge Program and over 860 chemicals sponsored indirectly through international efforts. With voluntary data collection nearing its conclusion, the focus of the HPV Challenge Program has shifted to data use, both by the public and by EPA in its mission to protect human health and the environment.

EPA IRIS. http://www.epa.gov/NCEA/iris/. The EPA Integrated Risk Information System (IRIS) is a database on human health effects that may result from exposure to chemicals in the environment. It was originally developed for EPA staff to meet a growing demand for consistent information for use in risk assessments. The database includes information on cancer effects and noncancer effects. Carcinogens are evaluated and described with a letter or phrase.

EPA's guidelines for evaluating the potential carcinogenicity of chemicals have been updated over the years to reflect increased understanding of ways chemicals may cause cancer. For a review of the terms and key words or classifications see http://www.epa.gov/opp00001/health/cancerfs.htm#terms. The current guidelines call for greater emphasis on characterization discussions for hazard, dose-response assessment, exposure assessment, and risk characterization, as well as the use of mode of action in the assessment of potential carcinogenesis. EPA does not have the resources to re-evaluate every chemical to determine how it would be described under new guidelines, and there is no reason to re-evaluate chemicals unless there is some new information that could change the basic understanding of that chemical.

1986 letter classification

A- Human carcinogen
B- Probable human carcinogen
B1- limited evidence from epidemiologic studies
B2- sufficient evidence from animal studies and inadequate evidence from epidemiologic studies
C- Possible human carcinogen
D- Not classifiable
E- Evidence of non-carcinogenicity for humans

1996 classification phrases: known/likely, cannot be determined, not likely
1999 draft classification phrases: carcinogenic to humans, likely to be carcinogenic to humans, suggestive evidence of carcinogenicity, inadequate data for an assessment, not likely to be carcinogenic to humans
2005 classification phrases: carcinogenic to humans, likely to be carcinogenic to humans, suggestive evidence of carcinogenic potential, inadequate information to assess, not likely to be carcinogenic to humans.

EPA IUR. http://www.epa.gov/oppt/iur/. The purpose of the Inventory Update Reporting (IUR) program is to collect quality screening-level, exposure-related information on chemical substances and to make that information available for use by EPA and, to the extent possible, due to data confidentiality claims, to the public. The IUR data are used to support risk screening,

assessment, priority setting and management activities and constitute the most comprehensive source of basic screening-level, exposure-related information on chemicals available to EPA. 2006 IUR database includes information on how much of a chemical is produced and where it is manufactured, and the industrial function. Manufacturers that have quantities of >300,000 lbs on site must report use in children's products (up to 14 years of age) and commercial and consumer product category or categories that best describe the commercial and consumer products in which the chemical is used.

EPA VCCEP. http://www.epa.gov/oppt/vccep/. The Voluntary Children's Chemical Evaluation Program (VCCEP) was called for by the 1998 Chemical Right to Know Initiative, the goal of which was to give citizens information on the effects of chemicals to enable them to make wise choices in the home and marketplace. VCCEP is the portion of that initiative that deals with risks to children. The EPA selected 23 chemicals to which children have a high likelihood of exposure. Companies have agreed to provide information on health effects, exposure risk and data needs for 20 chemicals.

EPA PBT Profiler. http://www.epa.gov/oppt/sf/tools/pbtprofiler.htm. The PBT Profiler is an online risk-screening tool that predicts a chemical's potential to persist in the environment, bio-concentrate in animals, and be toxic, properties which cause concern for human health and the environment.

EU Chemical Regulations. http://ecb.jrc.ec.europa.eu/esis/. The new EU regulation on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) affects the previous EU chemical regulations. Until the new REACH regulation is fully implemented, the older regulations are also in effect. The European Chemical Substances Information System (ESIS) currently provides information on chemicals from different EU directives and information sources. Information for a given chemical includes classification on reproduction, mutagenicity and carcinogenicity, priority lists, and risk assessments.

EU Classifications are done based on their directives on classification, labeling and packaging (CLP). The classifications and categories are described in Annex VI of the Dangerous Substances Directive 67/548/EEC http://ecb.jrc.ec.europa.eu/documents/Classification-Labelling/DIRECTIVE_67-548-EEC/Annex_VI.pdf

Carcinogenic substances
Category 1: Substances known to be carcinogenic to man based on sufficient evidence in humans.
Category 2: Substances which should be regarded as if they are carcinogenic to man, usually based on sufficient evidence in long-term animal studies.
Category 3: Substances which cause concern for man owing to possible carcinogenic effects but the available information is not adequate for making a satisfactory assessment. This category includes chemicals which have been well investigated, but for which the evidence is insufficient for classification in category 2 and chemicals which are insufficiently investigated.

Mutagenic substances
Category 1: Substances known to be mutagenic (i.e., heritable genetic damage) to man based on sufficient evidence in humans.
Category 2: Substances which should be regarded as if they are mutagenic to man, usually based on sufficient evidence in animal studies.

Category 3: Substances which cause concern for man owing to possible mutagenic effects. There is evidence from appropriate mutagenicity studies, but this is insufficient to place the substance in category 2.

Substances toxic to reproduction
Category 1: Substances known to impair fertility or cause developmental toxicity in humans based on sufficient evidence in humans.
Category 2: Substances which should be regarded as if they impair fertility or cause developmental toxicity in humans, usually on the basis of clear results in animal studies.
Category 3: Substances which cause concern for human fertility or possible developmental toxic effects, generally on the basis of results in animal studies, but where the evidence is insufficient to place the substance in category 2.

EU Endocrine Disruptors.
http://ec.europa.eu/environment/endocrine/strategy/substances_en.htm. In 1999 the European Commission adopted a Communication on a Community Strategy for Endocrine Disrupters. The strategy focuses on man-made substances, including chemicals and synthetic hormones, which may cause cancer, behavior changes, and reproductive abnormalities. Substances were grouped into four major categories, described below. Only the first two categories were used in Phase 1 and Phase 2.

Category 1: Evidence of endocrine disruption activity in at least one species using intact animals
Category 2: Some *in vitro* evidence of biological activity related to endocrine disruption
Category 3: No evidence of endocrine disrupting activity or no data available

EWG. www.ewg.org. The Environmental Working Group (EWG) maintains a database on chemicals in cosmetics and sunscreen. In addition to information on toxicity, the database also includes information on how the product is used and who it is intended for. The data is gathered from retailers, manufacturers, and product labels. Companies that have signed the Campaign's Compact for Safe Cosmetics enter information into the database on ingredients, use and intended users. The products are not tested to determine if the information is accurate.

GHS. http://www.unece.org/trans/danger/publi/ghs/ghs_welcome_e.html. The Global Harmonized System of Classification and Labeling of Chemicals (GHS) is an internationally-harmonized approach to labeling and classification to ensure the safe use, transport and disposal of chemicals. GHS was developed by a committee of the United Nations and is being implemented around the world, including in the United States. GHS includes Safety Data Sheets (SDS's) based on GHS classifications for harmonized hazard communication. The Japanese Ministry of Economy, Trade, and Industry (METI) has classified 1500 chemicals using GHS. http://www.safe.nite.go.jp/english/ghs_index.html#results.

HSDB. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB. The Hazardous Substances Data Bank (HSDB) is part of the U.S. Department of Health and Human Services. HSDB is part of TOXNET, the Toxicology Data Network, which is a collection of databases on toxicology, hazardous chemicals, environmental health and toxic releases. HSDB contains comprehensive, peer-reviewed toxicology data for about 5,000 chemicals. Each record includes information on human and animal toxicity, chemical properties, manufacturing, and uses.

IARC. http://monographs.iarc.fr/ENG/Classification/index.php. The International Agency for Research on Cancer (IARC) is part of the World Health Organization (WHO). IARC publishes monographs on environmental factors that can increase the risk of cancer, including chemicals. Interdisciplinary working groups of expert scientists review the published studies and evaluate the weight of the evidence that an agent can increase the risk of cancer. The monographs include a categorization on carcinogenic risks to humans, which are listed below.

Group 1: carcinogenic to humans.
Group 2A: probably carcinogenic to humans.
Group 2B: possibly carcinogenic to humans.
Group 3: not classifiable as to its carcinogenicity in humans.
Group 4: probably not carcinogenic to humans.

NHANES. http://www.cdc.gov/nchs/nhanes.htm. The National Health and Nutrition Examination Survey (NHANES) is a collection of U.S. population biomonitoring studies which are representative of the population. There are many other biomonitoring studies, but they may not be representative of the US population. In addition to the NHANES report, we also used papers published between reports that use the survey data.

NLM Household Products Database. http://hpd.nlm.nih.gov/. The National Library of Medicine (NLM) Household Products Database is part of the U.S. Department of Health and Human Services and is also part of TOXNET, the Toxicology Data Network, which is a collection of databases on toxicology, hazardous chemicals, environmental health and toxic releases. The database links over 9,000 consumer brands to health effects from Material Safety Data Sheets (MSDS's) provided by manufacturers. MSDS's are required by the Occupational Health and Safety Administration (OSHA) and their target audience is the worker who may be exposed to chemicals at work. However, the information may also be relevant to consumers. The database contains information on which products contain specific chemicals and how much of the chemical is used in the product. The products are not tested to determine if the information is accurate.

NTP. http://ntp.niehs.nih.gov/. The National Toxicology Program (NTP) is an interagency program managed by the U.S. Department of Health and Human Services whose mission is to evaluate agents of public health concern by developing and applying tools of modern toxicology and molecular biology. The NTP has identified chemicals which pose a threat to human reproduction and which are known or suspected carcinogens. NTP's biennial Report on Carcinogens lists known or reasonably anticipated human carcinogens.

NTP CERHR. http://cerhr.niehs.nih.gov/reports/index.html. The NTP Center for Evaluation of Risks to Human Reproduction (CERHR) publishes monographs that assess evidence that environmental chemicals, physical substances, or mixtures cause adverse effects on reproduction and development in humans. The evaluations are done by panels of scientists and include a conclusion about the hazard.

REPROTEXT. http://csi.micromedex.com/X/Rera.htm. REPROTEXT is a commercial database from Thomson Reuters that reviews the full range of health effects of industrial chemicals commonly encountered in the workplace. It describes the effects on reproduction and development and gives each chemical a letter rating for reproductive hazard.

A+ human reproductive hazard with no known no-effect dose
A human reproductive hazard with known no-effect dose
A- unconfirmed human reproductive hazard
B+ multiple reproductive effects in animals but no human data
B mixed reproductive effects in animals but no human data
B- few reproductive effects in animals but no human data
C no reproductive data found
D insufficient information to identify
E known not to affect animal reproduction but no human data
F known not to affect human reproduction

RTECS. http://www.cdc.gov/niosh/rtecs/default.html. The Registry of Toxic Effects of Chemical Substances (RTECS) is a comprehensive collection of toxicity data from the scientific literature. The data are presented in a standard format with links to the primary literature. The initial database was built and maintained by the National Institute of Occupational Safety and Health (NIOSH), which is part of the U.S. Department of Health and Human Services. RTECS is now updated and available commercially.

WA PBT list in the 2006 PBT Rule (173-333 WAC). http://www.ecy.wa.gov/programs/swfa/pbt/list.html. This list consists of 73 chemicals that are persistent, bioaccumulative, and toxic. The PBT Rule includes specific criteria for persistence, bioaccumulation and toxicity. A chemical is considered persistent if its half-life is at least 60 days in water, soil, or sediment. A chemical is considered to bioaccumulate if it has a bioconcentration factor or bioaccumulation factor greater than 1,000 or if its log-octanol water partition coefficient is greater than 5. A chemical is considered to have the potential to be toxic if it is a carcinogen, developmental or reproductive toxicant, or a neurotoxicant, the reference dose or equivalent is less than 0.003 mg/kg/day, or it has a chronic no observed effect concentration (NOEC) or equivalent that is less than 0.1 mg/L or an acute no observed effect concentration (NOEC) or equivalent that is less than 1.0 mg/L.

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